UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL No. 2327**
THIS DOCUMENT RELATES ONLY TO: **WAVE ONE PROLIFT, PROLIFT+M AND PROSIMA CASES LISTED ON EXHIBIT A**	**JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION TO EXCLUDE THE OPINIONS AND TESTIMONY OF RUSSELL DUNN, PH.D., P.E.[1]

Defendants Ethicon, Inc. and Johnson & Johnson (collectively, "Ethicon") submit this memorandum in support of their motion to exclude the opinions and testimony of Russell Dunn, Ph.D., P.E., Plaintiffs' chemical engineering expert.[1]

I. INTRODUCTION

Dr. Russell Dunn is a Professor in the Department of Chemical and Biomolecular Engineering at Vanderbilt University. Plaintiffs designated Dr. Dunn to offer opinions (a) that Ethicon's Prolene mesh used in its Prolift, Prolift+M, and Prosima medical device systems for repair of pelvic organ prolapse undergoes hazardous oxidative degradation in vivo and (b) that Ethicon's quality system, including design, quality controls, and risk management, for these devices failed to comply with industry standards. Ex. B, Dunn Report. The Court should exclude Dr. Dunn's opinions under *Daubert* because (a) he is not qualified to offer opinions on in vivo

[1] The specific cases to which this memorandum relates are listed in Ex. A. All exhibits referenced herein are attached to Ethicon's accompanying motion.

degradation of Ethicon's Prolene and/or the design, quality control, or risk management of these pelvic mesh medical devices, (b) his opinions are not reliable, and (c) his opinions are not relevant.

Prior to becoming involved with the pelvic mesh litigation, Dr. Dunn had no experience with medical devices. He admits that he is not an expert in biomaterials. Dr. Dunn has never been involved in the design, quality controls, and/or any aspect of risk management of any medical device. Moreover, Dr. Dunn has no experience with the medical industry standards that are the subject of his opinions, and he has a serious misunderstanding of those standards. Because of this misunderstanding, he failed to consider Ethicon's risk management addressing the subject of oxidative degradation that is the foundation for all of his opinions.

II. LEGAL STANDARD

Ethicon incorporates by reference the standard of review for *Daubert* motions as articulated by the Court in *Edwards v. Ethicon, Inc.*, 2014 WL 3361923, at *1-3 (S.D.W. Va. July 8, 2014).

III. ARGUMENT AND AUTHORITIES

A. Dr. Dunn Is Not Qualified

1. Dr. Dunn has no experience with medical devices

The essence of Dr. Dunn's report is that Ethicon's Prolene undergoes oxidative degradation in the body, that the oxidative degradation is a hazard that cannot be eliminated, and that Ethicon's quality system and risk management is deficient because it did not eliminate this "hazard." *See generally* Ex. B, Dunn Report. However, Dr. Dunn's doctoral thesis dealt with waste minimization -- totally unrelated to medical devices or the way polypropylene behaves in the body. Ex. C, Dunn 11/20/15 Dep. Tr. 249:18-250:6. Dr. Dunn has never worked with medical implant devices other than this litigation. *Id*. at 241:23-242:3. He has no experience in

the design or manufacture of a medical device. *Id*. at 242:4-22. He has never consulted for a medical device manufacturer. *Id*. at 242:23-25. Dr. Dunn has never taught a course on medical devices. *Id*. at 243:5-245:9. He has never published an article or book concerning a medical device. *Id*. at 248:25-249:7, 250:21-24. Dr. Dunn has never published in a medical journal. *Id*. at 252:8-10. His only work experience with polypropylene behavior in vivo is in this mesh litigation. *Id*. at 250:25-251:12. Dr. Dunn has been retained as an expert more than 100 times, but never for a medical device until this litigation. *Id*. at 251:13-252:7. None of Dr. Dunn's 15 publications and 19 presentations listed in his CV relate to a medical device. Ex. D, Dunn CV.

Moreover, Dr. Dunn admits that he is not qualified to opine whether Prolene does in fact undergo oxidative degradation in the body. Ex. C, Dunn 11/20/15 Dep. Tr. 54:7-55:20. Dr. Dunn concedes that he is not qualified to opine whether oxidative degradation of Prolene has any effect in the human body. *Id*. at 43:10-19. More specifically, he acknowledges that he has no expertise to evaluate whether oxidative degradation of Prolene has any effect on tissue in the body. *Id*. at 64:6-9. Additionally, Dr. Dunn concedes that he has no expertise to opine whether oxidative degradation of Prolene in the body has the potential to cause any harm.[2] *Id*. at 69:13-70:4. Dr. Dunn has no expertise relating to biocompatibility. *Id*. at 307:7-9; Ex. E, Dunn 3/7/16 Dep. Tr. 126:10-24. In fact, he does not even know what a biocompatibility risk assessment is.[3] Ex. C, Dunn 11/20/15 Dep. Tr. 70:5-14.

[2] Dr. Dunn's admitted lack of expertise regarding "harm" is critical because the thrust of his report is that oxidative degradation is a "hazard," but he ignores the definition of "hazard" which is a "potential source of harm." *See* Section III.B.3, below.

[3] Dr. Dunn's admitted lack of expertise regarding biocompatibility risk assessments is critical because these assessments are the industry standard means by which to assess oxidative degradation. *See* Section III.A.2, below.

This Court has previously written concerning Dr. Dunn's "complete lack of experience with medical devices outside of litigation" and concluding that his opinions would not be helpful to the trier of fact. *Mathison v. Boston Scientific Corporation*, 2015 WL 2124991, at *21-22 (S.D. W.Va. May 6, 2015). The same conclusion should be reached in this case.

2. Dr. Dunn lacks expertise in the applicable standards for assessing oxidative degradation of a medical device

Dr. Dunn cites ISO 14971 as the only written medical industry standards on which he bases his opinions concerning Ethicon's risk management generally and assessment of oxidative degradation in particular. Ex. E, Dunn 3/7/16 Dep. Tr. 15:14-16:8. Dr. Dunn is not aware of other applicable standards discussed below. However, at the outset it should be noted that Dr. Dunn never even read ISO 14971 until January 2014, that is, after he was retained as an expert in this litigation. Ex. C, Dunn 11/20/15 Dep. Tr. 31:19-23; Ex. F, Dunn 2/21/14 Dep. Tr. 112:6-16. Dr. Dunn has never performed a risk analysis applying ISO 14971. Ex. C, Dunn 11/20/15 Dep. Tr. 31:24-32:14. In fact, Dr. Dunn has never even participated on a team performing an FMEA relating to any medical device. Ex. E, Dunn 3/7/16 Dep. Tr. 126:1-9.

Both ISO 14971:2000 and ISO 14971:2007 specifically direct that the reader refer to ISO 10993 for guidance on the general principles for biological evaluation, or biocompatibility, of medical devices. Ex. G, ISO 14971:2000 at 26-27; Ex. H, ISO 14971:2007 at 76-77. This expressly includes risk analysis concerning the "chemical nature of the materials" and the "influence of biodegradation." Ex. G, ISO 14971:2000 at 26; *see also* Ex. H, ISO 14971:2007 at 76. In contrast, Dr. Dunn believes there are no published standards for testing, or otherwise assessing risks, for potential chemical hazards. Ex. E, Dunn 3/7/16 Dep. Tr. 92:13-95:7. Dr. Dunn says he has heard of ISO 10993, but admits that he does not know what it is and has never

used it. Ex. C, Dunn 11/20/15 Dep. Tr. 24:24-25:9, 188:18-189:9; *see also* Ex. I, ISO 10993-1:1997; Ex. J, ISO 10993-9; Ex. K, ISO 10993-13. In explaining the reason biocompatibility risk assessments are not considered in his report, Dr. Dunn goes so far as to declare that ISO 10993 does not even address oxidative degradation. Ex. C, Dunn 11/20/15 Dep. Tr. 186:9-187:10. The face of the various parts of ISO 10993 plainly reveals that Dr. Dunn is seriously mistaken:

Introduction

This part of ISO 10993 was developed from ISO/TR 10993-9. Degradation products covered by this standard are formed primarily by chemical bond scission due to hydrolytic and/or oxidative processes in an aqueous environment. It is recognized that additional biological factors, such as

. . . .

3 Definitions

. . . .

3.5 oxidative degradation
scission of chemical bonds in a polymer by the attack of oxidizing agent(s)

. . . .

NOTE The accelerated degradation test may be used as a screening test. If no degradation is observed in the accelerated test, no real-time degradation test should be necessary.

. . . .

4.1.4.1.2 Reagents for oxidative degradation

For oxidative degradation the following solutions are suggested:

a) water and hydrogen peroxide, e.g. 3 % hydrogen peroxide solution, Pharmacopoeia grade;

b) Fenton´s reagent [mixture of dilute hydrogen peroxide solution and iron(II) salts, e.g. 100 µmol Fe^{2+} and 1 mmol H_2O_2].

Ex. K, ISO 10993-13 at v, 2-3. Again, Dr. Dunn's lack of knowledge of the relevant industry standards should disqualify his opinions.

3. Dr. Dunn is not qualified to opine regarding Ethicon's quality systems

Dr. Dunn opines that Ethicon's quality systems for Prolift, Prolift+M, and Prosima are "inadequate." Ex. B, Dunn Report at 30.[4] As an example, Dr. Dunn opines that Ethicon does not adequately address complaint handling. *Id*. However, he testified that there are no written industry standards addressing quality systems for the design of medical devices. Ex. C, Dunn 11/20/15 Dep. Tr. 19:12-22:4. Instead, he says that his opinions concerning Ethicon's quality systems are based solely on general engineering principles that he teaches to chemical engineers. *Id*. at 21:6-22:4.

Dr. Dunn has never heard of 21 CFR Part 820, that is, the specific regulations that govern quality systems, including complaint handling, for medical devices in the United States. *Id*. at 22:5-23. He has never heard of Medical Directive 93/42/EEC, the European regulations governing quality systems, including complaint handling, for medical devices. *Id*. at 24:11-13. Dr. Dunn has never heard of ISO 13485, the industry standard adopted in the EU for medical device quality systems, including complaint handling. *Id*. at 24:14-23; Ex. L, ISO 13485:2003. Dr. Dunn's report nowhere mentions Ethicon's own internal quality systems procedures which are designed, in part, to meet the requirements of ISO 13485:2003. Ex. M, PR800-011 Version 4.

This is not surprising because Dr. Dunn has never participated in the development of a quality system for a medical device. Ex. C, Dunn 11/20/15 Dep. Tr. 49:6-14. He has no experience in maintaining, or even auditing, a quality system for a medical device. *Id*. at 51:20-52:5. He has never taught a course on the development of a quality system for a medical device.

[4] Dr. Dunn did not number the pages of his report. Thus, page number references to his report are determined manually by counting the pages.

Id. at 49:15-21. A key component for a quality system for the design and development of a medical device is design controls, in particular as design controls address risk analysis, but Dr. Dunn has never participated in preparing design controls for a medical device. *Id*. at 52:24-53:4. In fact, he has no idea what the required design control processes are for the design and development of a medical device.[5] *Id*. at 49:22-50:23. Moreover, Dr. Dunn is not aware of any medical industry standards for complaint handling and analysis.[6] *Id*. at 66:14-17.

Dr. Dunn should not be permitted to opine regarding Ethicon's quality systems, including complaint handling, because he does not even know the applicable standards by which Ethicon should be judged.

4. Dr. Dunn is not qualified to opine whether Ethicon's assessment of biocompatibility, including oxidative degradation, is adequate

Dr. Dunn opines that Ethicon's assessment of oxidative degradation is deficient. Ex. B, Dunn Report at 4, 17, 19. However, he lacks the expertise to evaluate Ethicon's assessment against the applicable industry standards. Both ISO 14971 and ISO 10993 explain that key factors in assessing biocompatibility include study of history of clinical use and existing biological safety data. Ex. H, ISO 14971:2007 at 76; Ex. I, ISO 10993-1:1997 at 3, 7, 10; Ex. J, ISO 10993-9, iv, 2. Even Dr. Dunn admits that a literature review is a tool for assessing the risk of oxidative degradation. Ex. C, Dunn 11/20/15 Dep. Tr. 78:24-79:7. However, Dr. Dunn candidly acknowledges that he has no expertise in these areas. *Id*. at 237:10-238:14. Thus, it is not appropriate for Dr. Dunn to opine as to the adequacy of Ethicon's assessment of

[5]The design control processes are a key portion of a quality system as it relates to product design and development and are specifically described and mandated in both 21 CFR Part 820.30 and Section 7.3 of ISO 13485:2003, Ex. L.

[6]Complaint handling and analysis standards are specifically described and mandated in both 21 CFR §820.100 and §820.198, as well as Section 8 of ISO 13485, Ex. L.

biocompatibility. Moreover, since the assessment of biocompatibility necessarily includes the assessment of degradation, Dr. Dunn should not be permitted to opine concerning Ethicon's assessment of degradation.

B. Dr. Dunn's Opinions Are Not Reliable

As explained below, Dr. Dunn's lack of experience relating to quality systems and risk management of medical devices led him to express opinions that are not reliable.

1. Dr. Dunn's opinions are not reliable because he misapplies ISO 14971 and thus fails to consider Ethicon's biocompatibility analyses

a. Dr. Dunn's opinions concerning FMEAs are flawed

Dr. Dunn purports to rely upon ISO 14971 to support his opinions that Ethicon's risk management was deficient. Ex. B, Dunn Report at 21-24, 27-29. However, his report and deposition testimony reveal important misapplications of this standard. ISO 14971 defines a "risk analysis" as a "[s]ystematic use of available information to identify hazards and to estimate risk." Ex. G, ISO 14971:2000 at 14; *see also* Ex. H, ISO 14971:2007 at 4. Nowhere in ISO 14971 is there any requirement that risk analysis be documented in any particular format. Note 2 under Section 4.1 of ISO 14971 references merely as examples "some risk analysis techniques are described in Annex G."[7] Ex. H, ISO 14971:2007 at 9. An FMEA format is but one of the *sample* techniques listed in Annex G. *See id.* at 56-59.

More importantly to the case at hand, Note 4 under Section 4.1 specifically refers the reader to Annex I for "risk analysis techniques for toxicological hazards."[8] *Id.* at 9. Annex I does not reference an FMEA at all. Annex I specifically addresses "the chemical nature of the materials," and "the influence of biodegradation" in particular, and refers the reader to ISO

[7]Ex. G, ISO 14971:2000, at 18, contains a similar reference to its Annex F.
[8]Ex. G, ISO 14971:2000, at 18, contains a similar reference to its Annex C.

10993 for further guidance on the risk analysis techniques. *Id*. at 76. As explained below, Ethicon followed these standards in considering the potential impact for any degradation of Prolene as part of its various risk analyses and biocompatibility risk assessments conducted for its Prolene mesh products, but Dr. Dunn fails to consider Ethicon's risk assessments.

Contrary to these specific provisions of ISO 14971, a central theme of Dr. Dunn's report and opinions is that the only way to document consideration of "oxidative degradation" is to have an express entry using those two specific words in an FMEA, and only in an FMEA. Ex. B, Dunn Report at 24, 30. In fact, Dr. Dunn testifies:

> Q. Well, in connection with forming your opinions on whether or not Ethicon has support for its belief that oxidative degradation is not an issue, I mean, did you try to look at any depositions --
>
> A. It is unnecessary. If it was considered, it will be in the FMEA. Bottom line. Doesn't matter who testified about it. They can say whatever they want to. If it's not in the FMEA, it was not considered.
>
> Q. Okay. What if it's in the risk analysis that is referenced in the FMEA? Does that mean they considered it or does it mean they did not consider it?
>
> A. Are you talking about the device design safety assessment?
>
> Q. I want to go back to Exhibit 10, yes.
>
> A. Okay.
>
> Q. Question Number 10 again.
>
> A. You're talking about a question. You're not talking about an actual analysis. You're talking about a question. Okay. Go ahead.
>
> Q. You see it refers you to the Gynemesh PS design history file as support for their answer that they have considered the biocompatibility.
>
> A. Yes.

> Q. Okay. So, if that reference takes you to a risk assessment for the biocompatibility that includes oxidative degradation, then you would have to stand corrected?
>
> A. No.
>
> Q. Oh. Okay.
>
> A. You don't have to go and fight through the weeds to figure out what's been done as an adequate safety analysis. I teach failure mode and effects analysis. It will be listed on the document if it's considered.
>
> Q. Are you telling the jury that ISO 14971 does not allow reference to other documents?
>
> A. That's not what I said.
>
> Q. Okay.
>
> A. I said, if it's considered as a potential failure mode, it will be listed on the failure mode and effects analysis. And of course it references other documents. But, if it was considered as a potential failure mode, it will be listed on the FMEA.

Ex. E, Dunn 3/7/16 Dep. Tr. 116:15-118:12; *see also id.* at 53:14-54:7. A fundamental flaw in Dr. Dunn's position is that there is no requirement anywhere in ISO 14971 that risk analysis be in the form of an FMEA. Plaintiffs' own expert, Anne Wilson, concedes this point. Ex. N, Wilson 3/22/16 Dep. Tr. 47:22-48:8.

Another fundamental flaw is that ISO 14971 does not require the use of the specific term "oxidative degradation" in a risk analysis. Nowhere in either his report or his deposition testimony does Dr. Dunn cite any standard for his opinion that risk analysis can only be performed in the form of an FMEA or that the specific term "oxidative degradation" must be used.

Yet another fundamental flaw in Dr. Dunn's analysis is that he even goes so far as to opine that throughout the life of the device when new post-production information concerning potential hazards is received, then the FMEA is a "living" document that requires Ethicon to go

back and formally update the FMEA instead of using any other technique for assessing a new potential hazard. Ex. C, Dunn 11/20/15 Dep. Tr. 170:1-171:12. There is no requirement anywhere in ISO 14971 that an FMEA be a living document for the entire life of the device.

In a nutshell, Dr. Dunn is opining that form takes complete and total precedence over substance, and yet he offers no industry standard to support such a proposition. When confronted with the actual language of ISO 14971, Dr. Dunn admitted that ISO 14971 does not require post production information to go back into an FMEA, but he then opined that ISO 14971 is wrong and needs to be changed because in his view an FMEA is the only way to assess risks. Ex. C, Dunn 11/20/15 Dep. Tr. 176:17-177:19. Dr. Dunn's stubborn defiance of ISO 14971 alone should render his opinions unreliable.

b. Dr. Dunn fails to consider Ethicon's biocompatibility analyses

Because of his mistaken views of ISO 14971, Dr. Dunn fails, and indeed refuses, to consider Ethicon's important work documenting its consideration of "biocompatibility." Ex. E, Dunn 3/7/16 Dep. Tr. 116:15-118:12; *see also id.* at 53:14-54:7. According to both ISO 14971 and ISO 10993, "biocompatibility" includes all forms of chemical degradation. Ex. H, ISO 14971:2007 at 76; Ex. I, ISO 10993-1:1997 at 2, 4, 7; Ex. J, ISO 10993-9:1999; Ex. K, ISO 10993-13:1999. Ethicon has reviewed the biocompatibility of its Prolene mesh many times. First, the risk analysis for the Prolift device referenced in the testimony quoted above, while not exactly in the form of an "FMEA" required by Dr. Dunn's invented criteria, included the following entries which Dr. Dunn refuses to consider since this was not a formal FMEA and since they did not use the precise words "oxidative degradation":

CHARACTERISTIC	ISSUE	RESPONSE N/A	RESPONSE YES	COMMENT

3 Materials	9) Define the materials utilized in the construction of the device. Highlight those materials that will involve direct patient contact		Yes	• **Guide**
				  • Handle – Polycarbonate
				  • Needle – Stainless Steel 316 LVM
				• **Cannula**
				  • Cannula - Pebax and TiO_2
				  • Hub - Pebax and TiO_2
				• **Retrieval line**
				  • Monofilament –Polypropylene
				  • Heat Shrink – Polyolefin
				  • Seal – Silicone elastomer (MED6015)
				• **Mesh**
				  • GYNECARE GYNEMESH PS mesh – PROLENE Polypropylene

	10)Have the materials been tested for toxicity and biocompatability?		Yes	If yes, please identify where the file(s) are located. • Cannula, Guide, Retrieval Device – Reference Gynecare PROLIFT eDHF (DHF0000105) • Mesh – Reference GYNECARE GYNEMESH PS mesh DHF #0956
	11)Have the materials been tested for carcinogenicity, teratology, and mutagenicity (as appropriate)?		Yes	If yes, please identify where the file(s) are located. • Cannula, Guide, Retrieval Device - Reference Gynecare PROLIFT eDHF (DHF0000105) • Mesh – Reference GYNECARE GYNEMESH PS mesh DHF #0956
	12)Is the strength of load-bearing materials sufficient for the intended use?		Yes	If yes, please attach test data or engineering analysis Reference Gynecare PROLIFT eDHF (DHF0000105), Design Verification

Ex. O, 2005 Prolift DDSA at Appendix III, pp. 2-3. The reader is referred to "DHF #0956" for further assessment of biocompatibility, but Dr. Dunn's report does not address this file or the risk assessment contained in the file.

Similarly, the risk analysis for the Prosima device stated on its face that it does not cover the properties of the mesh but rather applied ISO 14971, Section 4.1, Notes 1 and 5, and Annex A.2.4.1 by referencing the same "GYNEMESH PS mesh DHF #0956" for the documentation of biocompatibility analysis. Ex. P, 2007 Prosima dFMEA at 15; Ex. H, ISO 14971:2007 at 9. The standards encourage such a reference because the Gynemesh PS material was identical to the Prolift and Prosima material. Ex. G, ISO 14971:2000 at 18; Ex. H, ISO 14971:2007 at 19. The risk analyses in the referenced file "DHF #0956" expressly included the following pertinent entries:

ACTIVITY	YES/NO/NA	FILE REFERENCE	COMMENT
Long term use of equivalent product has been considered from both the positive and negative perspective. Clinical/Scientific reports, both internal and published: Device failure reports:	YES	Re: Clinical and Scientific reports	Raw Materials and Indications for device similar to the Soft PROLENE mesh
The contact conditions and timing with the patient have been considered.	YES.	Re: Clinical and Scientific reports	Raw Materials and Indications for device similar to the Soft PROLENE mesh
Materials and components used for fabrication and manufacture have been considered. Chemical nature, quantitative formulation, additives, processing aids, monomers, catalysts, residues: Concentration, availability, toxicity: Biodegradation aging and corrosion: Previous use of this material, and long term effectiveness in equivalent application can be demonstrated: Appropriate biocompatability testing to EN 30993:	YES	Ref: Soft PROLENE Mesh Biocompatibility Strategy	Raw materials are chemically unchanged – The Soft PROLENE Resins utilized in clear and blue pigmented sutures have been utilized in the fabrication of this mesh.

. . . .

DEVICE DESIGN SAFETY ASSESSMENT (DDSA) FORM

LINE NUMBER	HAZARD	SEVERITY of HARM	PROBABILITY of HAZARD	RISK LEVEL	FAULT CLASS	COMMENT	REFERENCES
1	Loss of Mechanical Integrity – Intraoperative	3	2	III	C	Clinical study design will assess this parameter	Ref.: Clinical Literature search
2	Loss of Mechanical Integrity – postoperative	3	1	II	C	Clinical study design will assess this parameter	Ref.: Clinical Literature search

Ex. Q, 2002 Gynemesh PS DDSA at 3, 14. These entries plainly show that Ethicon followed ISO 14971 and ISO 10993 in reviewing the history of safe clinical use of Prolene and the applicable clinical literature.

As noted in his testimony above, Dr. Dunn refuses to go beyond the FMEAs themselves to review the documents referenced in these and earlier risk analyses that also assessed the biocompatibility of the same mesh material. His opinions are unreliable because he fails, and in fact refuses, to consider the very documents that housed Ethicon's consideration of degradation. In order to provide a complete picture of Ethicon's analyses, one must review all of its many risk analyses, biocompatibility risk assessments and literature reviews dating back to 1995 because they all concern the exact same Prolene in the mesh material. *See generally* Ex. R, 1995 Prolene Mesh Risk Analysis; Ex. S, 1997 Prolene Mesh Risk Analysis, Biocompatibility Risk Analysis

and Literature Review; Ex. T, 1999 Prolene Soft Mesh Biocompatibility Risk Assessment; Ex. U, 2000 Prolene Soft Mesh Risk Analysis; Ex. V, 2000 Prolene TVT Mesh Biocompatibility Risk Assessment; Ex. W, 2001 Prolene TVT Mesh Risk Analysis; Ex. X, 2002 Gynemesh PS Biocompatibility Risk Assessment; Ex. Y 2005 Prolift Biocompatibility Risk Assessment; Ex. Z, 2007 Prosima Biocompatibility Risk Assessment; Ex. AA, March 2001 Literature Review; Ex. BB, May 2001 Literature Review; Ex. CC, 2007 Prolift+M Clinical Expert Report and Literature Review; Ex. DD, 2010 Gynemesh PS Clinical Expert Report and Literature Review.[9] Dr. Dunn's opinions are not reliable because his report does not discuss any of these risk analyses, biocompatibility risk assessments and literature reviews.

2. Dr. Dunn's opinions concerning testing are unreliable because he fails to apply ISO 10993

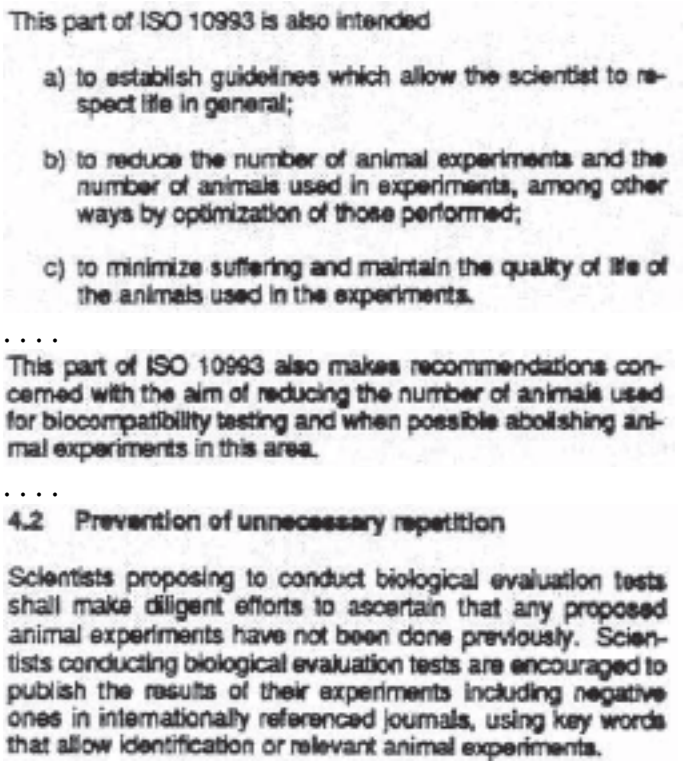
Dr. Dunn opines that one of the key shortcomings of Ethicon's risk management is that it failed to conduct more tests on Prolene to further study oxidative degradation. Ex. B, Dunn Report at 17, 19, 31. Dr. Dunn believes there are no published standards for testing, or otherwise assessing risks, for potential chemical hazards. Ex. E, Dunn 3/7/16 Dep. Tr. 92:13-95:7. Dr. Dunn again misunderstands and ignores ISO 10993.

As noted previously, ISO 14971 directs the reader that biocompatibility risk analysis, including the assessment of the potential impact of degradation, be performed under the general principles stated in ISO 10993. Ex. H, ISO 14971:2007 at 76-77. Both ISO 14971 and ISO

[9] Ethicon's Biocompatibility Risk Assessments reference both ISO 10993 and the FDA's Program Memorandum #G95 because that memorandum directs manufacturers as to what needs to be included in a biocompatibility risk assessment. *See* http://www.fda.gov/RegulatoryInformation/Guidances/ucm080735.htm. Defendants are well aware of the Court's admonition against references to FDA requirements, but Ethicon's biocompatibility risk assessments plainly show that one simply cannot fully evaluate the sufficiency of Ethicon's consideration of degradation without referring to Program Memorandum #G95.

10993 plainly state that degradation, which includes chemical degradation and oxidative degradation in particular, is a subset of "biocompatibility." *Id*. at 76 ("Some factors that can affect the ***biocompatibility*** of the material include . . . the influence of *degradation* . . . ." (emphasis added)). As noted previously, Dr. Dunn's broad opinion is that Ethicon failed to adequately consider oxidative degradation. His more specific opinion is that Ethicon should have performed more testing for any effects of oxidative degradation. Ex. B, Dunn Report at 17, 19. However, Dr. Dunn's failure to include any analysis of ISO 10993, and Ethicon's compliance with this standard, renders his opinions unreliable.

For example, both ISO 14971 and ISO 10993 caution that unnecessary testing should be avoided:



This part of ISO 10993 is also intended

a) to establish guidelines which allow the scientist to respect life in general;

b) to reduce the number of animal experiments and the number of animals used in experiments, among other ways by optimization of those performed;

c) to minimize suffering and maintain the quality of life of the animals used in the experiments.

. . . .

This part of ISO 10993 also makes recommendations concerned with the aim of reducing the number of animals used for biocompatibility testing and when possible abolishing animal experiments in this area.

. . . .

4.2 Prevention of unnecessary repetition

Scientists proposing to conduct biological evaluation tests shall make diligent efforts to ascertain that any proposed animal experiments have not been done previously. Scientists conducting biological evaluation tests are encouraged to publish the results of their experiments including negative ones in internationally referenced journals, using key words that allow identification or relevant animal experiments.

Ex. EE, ISO 10993-2 at 1-2; *see also* Ex. H, ISO 14971:2007 at 77. Ethicon's many biocompatibility risk assessments followed this standard by considering the voluminous

literature and past studies that demonstrated many years of safe use of Prolene mesh in the body. However, Dr. Dunn's report nowhere analyzes whether historical testing and available clinical literature are not already sufficient so as to justify his opinion that yet more testing is needed. Dr. Dunn cannot even say what additional testing Ethicon needed to perform, only that Ethicon should have performed "more" testing. Ex. C, Dunn 11/20/15 Dep. Tr. 81:19-82:11. Moreover, Dr. Dunn's opinion that more testing is needed is not based on any medical industry standard. *Id*. at 82:12-25. For these additional reasons, his opinions are unreliable.

3. Dr. Dunn's opinions are unreliable because he cannot associate any clinical harm with oxidative degradation

Dr. Dunn repeatedly opines that oxidative degradation of Prolene is a "known risk" or "hazard." Ex. B, Dunn Report at 19, 21, 22, 27. The terms "harm," "hazard," "risk" and "risk analysis" are well-defined in ISO 14971:

> "**Harm**" means "physical injury or damage to the health of people, or damage to property or the environment."
>
> "**Hazard**" means "potential source of harm."
>
> "**Risk**" means "combination of the probability of occurrence of harm and the severity of that harm."
>
> "**Risk Analysis**" means "systematic use of available information to identify hazards and to estimate risk."

Ex. H, ISO 14971:2007 at 1, 4; Ex. G, ISO 14971:2000 at 13-14. Dr. Dunn has difficulty articulating these straight forward definitions of harm and hazard. Ex. C, Dunn 11/20/15 Dep. Tr. 26:18-28:7 (harm), 28:8-29:6 (hazard).

Understanding these terms is very important in the context of Dr. Dunn's report because he repeatedly opines that oxidative degradation causes "harm" and is an actual "hazard." Ex. B, Dunn Report at 19, 21, 27. For example, he opines that "***known risks*** of the Prosima, Prolift and

Prolift+M products are not being mitigated . . . ." Ex. B, Dunn Report at 19. However, his report nowhere identified any harm, much less any risk, associated with oxidative degradation of Prolene in the body. Moreover, when pressed at his deposition, Dr. Dunn was not able to articulate any harm to a person associated with oxidative degradation of Prolene. Ex. E, Dunn 03/7/16 Dep. Tr. 32:10-34:21, 89:17-24 ("Q. Do you know whether there is any practical consequence to oxidative degradation of Prolene in the Prolene meshes that are the subject of your report once they're in the body? A. That's – that's not part of my report . . . ."). Dr. Dunn is not aware of any literature associating any clinical harm with oxidative degradation of Prolene. Ex. C, Dunn 11/20/15 Dep. Tr. 260:13-261:2.

Dr. Dunn's entire report is premised upon a mere assumption that any oxidative degradation of Prolene, no matter how minute, will cause some harm to women. His opinions are not reliable because he cannot identify any such harm and he cannot identify any clinical literature associating any harm with oxidative degradation of Prolene in the body.

4. Dr. Dunn's opinions concerning oxidation of Prolene in the body are not reliable

Dr. Dunn opines that oxidative degradation of Prolene in the body is a hazard. *See generally* Ex. B, Dunn Report. However, he acknowledges that he does not have the expertise to opine whether Prolene does in fact oxidize in the body. Ex. C, Dunn 11/20/15 Dep. Tr. 111:22-113:2. In addition, even if Prolene were to undergo some amount of oxidation in the body, Dr. Dunn cannot identify any degradation products of the oxidative degradation of Prolene. *Id*. at 53:11-54:3. Most importantly, Dr. Dunn cannot say how long it would take Prolene to undergo any oxidation in the body. *Id*. at 77:2-78:23, 83:2-22. In fact, he admits that he has not even studied this question. *Id*. Thus, it is rank speculation for Dr. Dunn's testimony to be associated

with the actual experiences of any of the Plaintiffs. Dr. Dunn's lack of expertise and failure to analyze how long it would take for Prolene to oxidize in the body render his opinions unreliable.

5. Dr. Dunn's opinions are not reliable because he applies the wrong standard for risk analysis

Dr. Dunn opines that "[t]he proper way for Ethicon to *completely eliminate* the hazard of oxidative degradation of the Prolene PP mesh component of its pelvic mesh device is to use a suitable polymer, other than Prolene-polypropylene . . . ." Ex. B, Dunn Report at 27 (emphasis added). Elsewhere in his report he opines that the risk of oxidative degradation cannot be eliminated. *Id*. at 4, 12, 18. Then he concludes that for this reason Ethicon's Prolene mesh material is "defective." *Id*. at 4, 17, 18, 19. These opinions should be excluded both because they are based on an incorrect standard and they invade the province of the jury.[10] ISO 14971 does not mandate that hazards be "completely eliminated."

Even if Dr. Dunn were correct that oxidative degradation is both a hazard for Prolene and cannot be eliminated, then he has completely ignored the next step of analysis that ISO 14971 requires. ISO 14971 requires that for risks that cannot be eliminated a risk/benefit analysis must be performed to determine whether the benefits outweigh the risk. Ex. H, ISO 14971:2007 at 12-13, 43-48. If the benefits outweigh the risks, then it would be entirely inappropriate to label the device "defective." The fundamental premise underlying ISO 14971 is that it is impossible to eliminate all risks from any medical device -- "'absolute safety' in medical devices [is] not achievable." *Id*. at v, 15. The risk/benefit analysis is critical because ISO 14971 requires that a medical device be deemed "safe[]" if it is "free[] from unacceptable risks." *Id*. at 4. Whether a

[10] Dr. Dunn's opinion that Prolene should not be used in Ethicon's pelvic organ prolapse devices should also be excluded because Dr. Dunn admits that he is not aware of a safer alternative. Ex. E, Dunn 3/7/16 Dep. Tr. 100:4-101:6.

risk is unacceptable is determined through a risk/benefit analysis. *Id*. at 12. An important element of a risk/benefit analysis is consideration of the state of the art for the medical device. *Id.* at 39. Dr. Dunn makes no attempt to evaluate the state of the art here. Ex. E, Dunn 3/7/16 Dep. Tr. 101:11-102:9.

Dr. Dunn's opinions are not reliable. Not only did he fail to perform a risk/benefit analysis, much less consider Ethicon's risk/benefit analyses, but he is unqualified to conduct or even evaluate a risk/benefit analysis for a medical device.

C. Dr. Dunn's Opinions Should Also Be Excluded Pursuant to Rule 403.

Even if the Court concludes that Dr. Dunn's opinions are relevant to this case and reliable—and they are neither—Dr. Dunn's testimony should still be excluded because any probative value it could have is substantially outweighed by the danger of unfair prejudice, confusion of the issues, and misleading the jury. *See* Fed. R. Evid. 403.

Evidence that is otherwise relevant still may be excluded if its probative value is substantially outweighed by the danger of unfair prejudice. Fed. R. Evid. 403. Evidence is unfairly prejudicial if it "would have an undue tendency to suggest a decision on an improper basis." *United States v. Stover*, Crim. A. No. 5:11-cr-00038, 2011 WL 4950369, at *2 (S.D.W. Va. Oct. 18, 2011) (citation omitted), *affirmed by* 499 F. App'x 269 (4th Cir. Dec. 14, 2012).

The probative value (if any) of Dr. Dunn's opinions regarding the safety and efficacy of polypropylene are substantially outweighed by the danger of unfair prejudice, confusion of the issues, and misleading the jury. Dr. Dunn did not conduct any tests on the Prolene mesh, and whatever validity his opinions possess is limited to generic polypropylene. But while Dr. Dunn's opinions are bereft of scientific support, his testimony is intended to cause the jury to infer that Prolene is synonymous with generic polypropylene, and therefore subject to the same alleged

degradation issues as generic polypropylene. **As previously noted, it is critical to observe that even if the jury were to believe that Dr. Dunn is correct that oxidative degradation can occur in Prolene in the body over time, Dr. Dunn admits that he has not studied, and has no idea, how much time it would take for any such degradation to occur. Thus, a jury determination that oxidative degradation played any part in any of the Plaintiffs' alleged injuries would be rank speculation.** Ultimately, the risk that Dr. Dunn's testimony could confuse or otherwise mislead the jury into assuming that his opinions pertaining to generic polypropylene also applied to Prolene far outweighs the limited probative value of Dr. Dunn's evidence. Accordingly, Dr. Dunn's opinion testimony also should be excluded due to its unfair prejudice, confusion of the issues, and potential to mislead the jury.

D. Dr. Dunn's Opinions Regarding Ethicon's Alleged Corporate Knowledge Or Intent Should Be Excluded.

In his report, Dr. Dunn relies on certain of Ethicon's internal documents to opine that Ethicon had certain corporate knowledge in the 1980s and 1990s and failed to assess risks relating to that knowledge properly before marketing its products. Ex. B, Dunn Report at 15-17. In accordance with this Court's prior rulings, Dr. Dunn's opinions regarding corporate knowledge and intent should be excluded. *See Mathison v. Boston Scientific Corporation*, 2015 WL 2124991, at *3 (S.D. W. Va., May 6, 2015).

IV. CONCLUSION

For the reasons set forth above, the Court should exclude the opinions and testimony of Dr. Dunn.

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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL No. 2327**
THIS DOCUMENT RELATES ONLY TO: **WAVE ONE PROLIFT, PROLIFT+M AND PROSIMA CASES**	**JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

CERTIFICATE OF SERVICE

I, William M. Gage, certify that on April 21, 2016, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notification of such filing to the CM/ECF participants registered to receive service in this MDL.

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